İKİ HAFTADA YEDİ PULMONER RENAL SENDROM OLGUSU. RPGN MEVSİMİ Mİ?

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ÖZET

Pulmoner renal sendrom genellikle diffüz alveoler hemoraji ve özellikle hızlı ilerleyen glomerulonefrit şeklindeki otoimmün glomerüler tutulumla ortaya çıkar. Hızlı ilerleyen glomerulonefrit ve/ veya pulmoner renal sendromun tedavisi zor olsa da, yüksek doz metilprednizolon, siklofosfamid gibi sitotoksik ajanlar ve plazmaferez hayat kurtarıcı olabilmektedir. Güçlü klinik kuşku varlığında, hastalığın erken dönemlerinde histopatolojik değerlendirme öncesi ve hatta yokluğunda erken tanı ve tedavi gereklidir. Lupus nefriti, Wegener granülomatozisi ve anti nötrofil sitoplasmik antikor ilişkili glomerülonefritlerin mevsimsel ortaya çıkma eğilimleri olduğu bilinmektedir. Farklı hastalıkların bu mevsimsel ortaya çıkma eğilimi, altta yatan patojenik tetikleyici faktörleri yansıtıyor olabilir.Yedi olgumuzun tümü ilkbahar döneminde ve iki haftalık süreç içinde kliniğimize başvurdu. Gözlemlerimiz, hızlı ilerleyen glomerulonefrit ve/ veya pulmoner renal sendromunun mevsimsel ortaya çıkma eğilimi olabileceği yönündedir.

Anahtar Sözcükler: Hızlı İlerleyen Glomerulonefrit, Pulmoner Renal Sendrom, Mevsim

SEVEN CASES OF PULMONARY- RENAL SYNDROME IN TWO WEEK. IS IT RPGN SEASON?

ABSTRACT

Pulmonary-renal syndrome (PRS) generally presents with diffuse alveolar haemmorhage (DAH) and autoimmune mediated glomerular involvement especially rapidly progressive glomerulonephritis (RPGN). Although treatment of RPGN and/or PRS is difficult, high dose methylprednisolone, cytotoxic agents such as cyclophosphamide and plasmapheresis can be life saving. Early diagnosis and treatment is necessary even in strong clinical suspicion at early stages of the diseases before or without histopathological evaluation. It is known that lupus nephritis, Wegener's granulomatosis, anti neutrophil cytoplasmic antibody (ANCA) associated glomerulonephritis have seasonal occurance tendency. Seasonal distributions of various diseases may reflect different pathogenic triggers that underly. All seven of our patients were addmitted to our clinic in two week period in early spring season. According to our observations, RPGN and/or pulmonary-renal syndromes may have a seasonal occurance tendency.

KEYWORDS: Rapidly Progressive Glomerulonephritis, Pulmonary Renal Syndrome, Season.

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INTRODUCTION

Rapidly progressive glomerulonephritis is a state of serious glomerular injury with clinical presentation of renal function loss among few days or weeks (1). Findings of glomerulonephritis such as hematuria, urinary erythrocyte cylinders and proteinuria are the main clinical presentations of RPGN. Main histological finding of this entity is crescent formation characterized with epithelial proliferation of Bowman's capsule, monocyte and macrophage infiltration in lesion area (2,3).

Crescentic glomerulonephritis can be idiopathic, can be due to various glomerular diseases, or can also be due to secondary to systemic diseases such as infections, systemic lupus, vasculitides (2). Couser et al. classified crescentic glomerulonephritis according to immune deposition as; Type 1- antiglomerular basement membrane disease, Type 2-immune complex disease, Type 3-pauci-immune type without any immune deposition (1). Medium and small vessel vasculitides with ANCA such as microscopic polyangiitis, Churg-Strauss syndrome and Wegener's granulomatosis affect kidneys and causes pauci-immune RPGN (4).

Clinical presentation of PRS consists of diffuse alveolar haemmorhage and autoimmune mediated glomerular involvement. Pulmonary renal-syndrome , characterized by a combination of DAH and RPGN, is caused by varied etiologies, including Goodpasture's syndrome, ANCA-associated small vessel vasculitis, cryoglobulinemia, systemic lupus erythematosus, environmental factors, and certain drugs (5-8).

Although treatment of RPGN is difficult, high dose methylprednisolone, cytotoxic agents and plasmapheresis can be efficacious at least initial period of disease (9,10). Prognosis of patients with pauci-immune RPGN with serum creatinine levels more than 3 mg/dl and histologically more than 50 % crescent formation is relatively poor. Early diagnosis and treatment is necessary even in strong clinical suspicion at early stages of the diseases before or without histopathological evaluation (11,12).

Seven patients we present here were addmitted to our clinic during nearly in two week period on early spring season. In the light of our clinical experiences of past years, we ask a question: Do RPGN and/or pulmonary-renal syndromes have a seasonal occurance tendency?

CASE PRESENTATIONS

Case 1: In March 2013, a 46 year old man was admitted to Urology clinic because of lomber pain and a mass lesion determined incidentally. Because abdominal tomography was compatible with renal cell carcinoma, nephrectomy of left kidney was executed. Because of gout history he was taking colchicine regularly for 4 years. After his operation he used boiled water of stinging nettle (urtica dioica) for one week. After this period he admitted to emergency service because of general health status deterioration. A laboratory examination indicated that hemoglobin was 5.9 g/dl, serum urea 107 mg/dl, serum creatinine 4.54 mg/dl, CRP 19 mg/dl, erytrocyte sedimentation rate 145 mm/h. Urinalysis showed proteinuria 2+ and hematuria 3+. The red cell counts in the urinary sediment were elevated. Abdominal ultrasound showed right kidney was edematous with increased echogenicity. Her renal function worsened with serum creatinine increasing steadily from 4.54 mg/dL on admission to a peak of 9 mg/dL. RPGN was diagnosed by urinary findings and progressive loss of renal function. During his clinical follow-up hemoptysis started. Serologically anti-nuclear antibody (ANA) was positive, C3 and C4 levels were in normal range, p-ANCA was negative but c-ANCA was strongly positive (149.6 U/ml). Coalescent alveolar infiltrates and ground glass opacities were seen in chest roentgenogram as shown in Figure 1a. During this hemoptysis period his hemoglobin levels decreased. Because he had a single kidney but clinical suspicion was strong we started immunosuppressive therapy immediately without kidney biopsy. Therefore, the patient was started on 500 mg of methylprednisolone intravenously daily for 3 days and 1 mg/kg/day orally afterwards in combination with cyclophosphamide 500 mg intravenously. After this therapy and 4 hemodialysis sessions and with 10 units of fresh frozen plasma, creatinine levels started to decrease even without dialysis afterwards, radiographic findings improved as shown in Figure 1b.

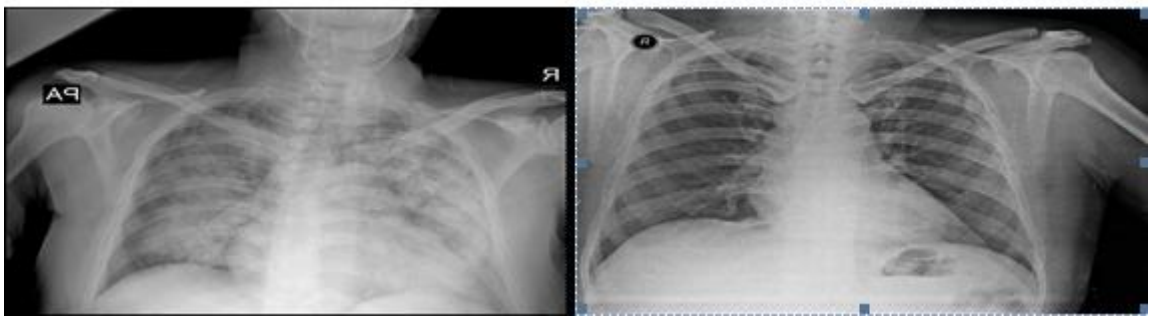

Figure 1: Chest X-Rays Of The Patient During Dah (A) And After Treatment (B).

Case 2: A 50 year-old woman with nausea, vomiting and peripheral edema admitted to our clinic. She had a history of elevated creatinine levels (2,5 mg/dl) nearly for 3 years. On admission laboratory tests indicated hemoglobin of 8.1 g/dl. Serum urea was 224 mg/dl, serum creatinine was 6.8 mg/dl, CRP was 14.5 mg/dl, erytrocyte sedimentation rate was 87 mm/h, albumin was 3.9 g/dl. Serologic markers were; p-ANCA > 100 U/ml, ANA (HEP 2) positive, c-ANCA negative, anti-GBM negative. During his follow-up hemoptysis started. Her hemoglobin levels decreased. Initial chest radiography showed perihilar opacities. Because of the refusal of the patient, renal biopsy and/ or bronchoscopy could not be executed. Microscopic polyangiitis and RPGN were diagnosed by serologic and urinary findings, progressive loss of renal function and pulmonary hemorrhage. After hemodialysis and fresh frozen plasma infusions her general status relatively ameliorated. Immediate corticotherapy and cyclophosphamide therapy were started and her dyspnea and hemoptysis decreased evidently.

Case 3: A 71 year-old man with dysuria, nausea and vomiting admitted to emergency service. On admission, tests indicated a hemoglobin of 9.3 g/dl. Urea was 120 mg/dl, serum creatinine was 5.7 mg/dl, CRP was 2.5 mg/dl, erytrocyte sedimentation rate was 50 mm/h, and albumin was 4.2 g/dl. Serologic markers were ANA negative, C3 and C4 levels in normal range, p-ANCA negative, c-ANCA positive (5.9 U/ml). He also had a history of dyspnea and haemoptysis. Because of his poor general status renal biopsy and/or bronchoscopy could not be executed. After hemodialysis his general status relatively ameliorated. Despite the routine anticoagulant and antiaggregant therapy, a central neurologic pathology with midbrain infarction was occurred.

Case 4: A 49 year-old woman with rheumatoid arthritis addmitted to our clinic with total anuria, oedema on pretibial area and petechial lesions on leg skin. On admission hematology tests indicated a hemoglobin of 7.4 g/dl. Urea was 107 mg/dl, serum creatinine was 6.3 mg/dl, CRP was 3.1 mg/dl, erytrocyte sedimentation rate was 51 mm/h, albumin was 2.3 g/dl. Serologic markers were, ANA negative, C3 and C4 levels in normal range , p/MPO-ANCA positive (8 U/ml), c/PR3-ANCA negative. After hemodialysis sessions we executed renal biopsy. In renal biopsy specimen, half of the glomeruli were concordant with cellular cresent formation without prominent immune staining (Fig. 2). After this result, firstly pulse

and than oral corticotherapy and after pulse steroid administration intravenous cyclophosphamide treatment were given to the patient. During her follow- up period urine amount did not increase and without hemodialysis her creatinine levels and peripheral oedema were increased, so routine hemodialysis planned for her.

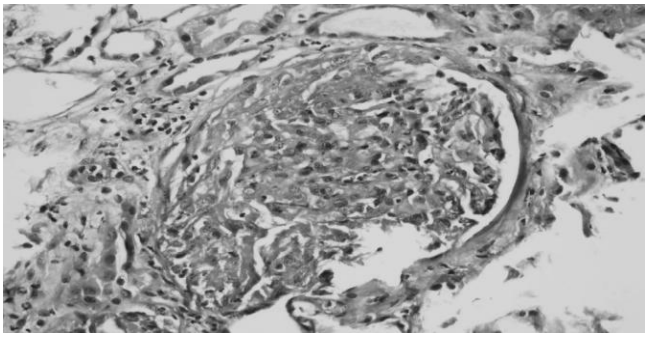

Figure 2: Cellular Crescent Formation In The Pathologic Specimen Of Patient 4

Other three patients were also similarly presented clinically with RPGN and cresent formation histopathologically. Despite the corticotherapy and cytotoxic treatment, two of them also progressed to ESRD that necessitates dialysis and one partially ameliorated with sustainig renal functional loss.

DISCUSSION

In addition to bilateral pulmonary infiltrates; renal failure necessitating haemodialysis, asthma attack, pericarditis, cerebral ischaemia, purpura, heart failure, falling haemoglobin levels, mononeuritis multiplex or polyarthralgia preoccupy PRS (13,14).

Because of especially pulmonary infectious complications, antibiotic treatment should be in mind in case of signs of infection in PRS cases (15). Although haemoptysis is the most common clinical sign of DAH due to PRS, low grade fever, cough, breathlessness are other clinical manifestations in this condition (16,17).

On the other hand most common renal findings comprise haematuria, proteinuria and active urinary sediment. If patients left untreated, this pathology can progress to end stage renal failure requiring dialysis (18). Chest roentgenograms and tomography are usefull to depict DAH (19). Coalescent alveolar infiltrates and consolidations with air bronchograms and sometimes ground glass opacities are common radiological findings of DAH. In 3-4 days complete roentgenographic resolution occurs during healing period with appropriate treatment

(20). In PRS situations proteinuria is nearly always present however not everytime in nephrotic range (18,20,21). Elevated serum urea, creatinine levels, oliguria, hypertension, oedema and anaemia are frequent in these patient group (20). Multiple coalescent shadows in chest roentgenograms with progressive haematocrit reduction strongly suggests DAH (17).

Diagnosis of PRS should be via lung or kidney tissue biopsy. In case of serious clinical problems, treatment should be started promptly even if histological evaluation is absent in order to preclude morbidity and mortality, if clinical suspicion is strong and ANCA or anti-GBM is positive (22-24).

Immunosuppressive therapy is essential for the treatment of ANCA-positive PRS. Induction therapy includes pulse methyl prednisolone (500-1000 mg) for 3-5 days and oral maintanance dose of 1 mg/kg for months. Corticotherapy may/should be combined with cytotoxic agents especially with cyclophosphamide (pulse intravenous administration at dose of 0.5-1 mg/m^2 per month or 1-2 mg/kg/day orally). Additionally plasma exchange should be in mind especially in serious conditions in order to restore renal functions (25,26).

It is clearly known that prevalence of class V and III lupus nephritis are common in winter and spring seasons (27). Also Wegener's granulomatosis, ANCA associated glomerulonephritis are reported to be more common in winter season. Seasonal distributions of various diseases may reflect different pathogenic triggers that underly. Seasonal fluctuations of immune system activity probably influenced by differentiations of some hormones such as glucocorticoids and melatonin, and leucocyte formule between seasons may be the underlying cause of the seasonality of some diseases, especially autoimmune disorders (28).

All seven of our patients were addmitted to our clinic in two week period in early spring season. Although renal biopsy could not be available for all of our patients, according to our observations, RPGN and/or pulmonary-renal syndromes may have a seasonal occurance tendency.

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